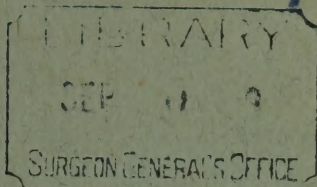


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CHANGES IN SKIN SENSITIVENESS TO TUBER-  
CULIN DURING EPIDEMIC INFLUENZA

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The disappearance of the cutaneous tuberculin reaction in [238] measles was systematically studied in 1908 by von Pirquet<sup>1</sup> following an observation of Preisich.<sup>2</sup> Fifty-nine children all failed to show skin sensitiveness during the exanthematic stage of the disease. A few observations made at the time of onset showed that the reaction disappeared for from one to four days before the eruption, to reappear gradually after from the fifth to the tenth day. Von Pirquet lays great stress on the specificity of the absence of the reaction in measles, pointing out that it does not disappear in scarlet fever, epidemic meningitis, typhoid fever or German measles. He associates the phenomenon with the tendency of tuberculosis to become more active after measles and explains it by assuming a disappearance of "ergins"—hypothetical substances which unite with tuberculin in the tissues to produce the reaction. Grüner<sup>3</sup> performed subcutaneous tests in children with measles and showed that with relatively large doses (1 mg.) a reaction could be elicited even during the eruptive stage. He calculated, however, that the skin sensitiveness was reduced about one thousand-fold. The observation of von Pirquet has been confirmed repeatedly in measles, but we have been unable to find reports of any similar constant abolition of tuberculin skin sensitiveness in other acute infectious diseases except during stages of agonal collapse.

During the recent epidemic of influenza we were struck by the remarkably low leucocyte counts encountered even in mild or ambulatory cases. This suggested that at least some of the [239] reactive processes of the body were in abeyance. It seemed of

[239] interest, therefore, to study skin sensitiveness in this disease. The present report deals with the results of cutaneous tuberculin tests in 19 consecutive cases of epidemic influenza studied in The Johns Hopkins Hospital during January and February, 1919. The diagnosis was based on the symptoms, the presence of hyperemic phenomena of the skin and mucous membranes, the character and duration of the febrile reaction, and the leucopenia.\* It should be emphasized that most of the cases were mild and that the disappearance of the skin reaction was in no way associated with general collapse. Three of the patients developed bronchopneumonia, but all made uneventful recoveries. None of them showed clinical signs of active tuberculosis.

Old tuberculin furnished by the tuberculosis dispensary of the hospital was used. Two drops were placed on the forearm about 5 cm. apart. Linear scarification with a dull scalpel was done through the drops of tuberculin after a control scratch had been made distal to them. The tuberculin was allowed to dry on the arm. The tests were all made by the same observers and read at one-, two- and three-day intervals, the character and extent of the redness and induration being noted. Tests were done during the febrile stage and after the temperature had become normal.

## RESULTS

The results of the tests are summarized in Table I. It is apparent that skin sensitiveness to tuberculin was absent in every case but one, both mild and severe, during the febrile stage. During convalescence reactivity returned in 89.4 per cent of the cases, which corresponds to what one would expect in a group of normal individuals of the same age. The return to maximum reactivity was gradual in most cases, as shown by successive tests. In two patients a positive skin test was not obtained during the period of observation, even after the temperature had been normal for from six to eight days.

It should be emphasized that, as in measles, more delicate tests, such as the subcutaneous, would probably show reactivity to be simply depressed and not entirely obliterated, and on this basis the cases may be divided into several groups. In ten

of them the first test made during the febrile stage failed to [239] elicit any sign of reaction, whereas during convalescence the test was markedly positive. In six cases in which the temperature became normal on the day on which the test was done, or on the following day, slight grades of reddening and induration appeared about the test scratches. These were regarded as delayed and depressed reactions, inasmuch as all these patients later responded with prompt, strongly positive reactions. It may be that in some of those cases the response was intensified by increased hypersensitiveness following the first test. In one instance of moderately severe typical influenza there was a positive test during the febrile stage. The same degree of reaction was observed in this patient during convalescence.

TABLE I  
SUMMARY OF RESULTS OF TUBERCULIN SKIN-TESTS IN EPIDEMIC  
INFLUENZA

	No.	Per cent.
Total cases studied .....	19	
Cases giving a positive reaction while fever was present .....	1	5.2
Cases giving a positive reaction after the febrile stage .....	17	89.4

Length of time (days) after tempera- ture had become normal before the skin test became positive	Number of cases
1	3
2	4
3	2
4	2
5	3
6	1
11	1

DISCUSSION

Although the literature on alterations of the skin test during acute infectious diseases is meager, it has been generally believed that measles stands out as the only disease in which a constant depression occurs. It is of interest, therefore, to find somewhat similar results in epidemic influenza. Beyond pointing out this fact, it seems difficult to associate the phenomenon in the two diseases, despite certain rather striking



[239] analogies which exist between them.\* It would seem wise, however, to restudy in detail the changes in skin sensitiveness in other acute febrile diseases, inasmuch as similar conditions may perhaps be found to exist.

#### REFERENCES

1. Von Pirquet: Deutsche med. Wchnschr., 1908, XXIV, 1297.
2. Preisich: Quoted by von Pirquet, *loc. cit.*
3. Grüner: Münch. med. Wchnschr., 1909, LVI, 1681.
4. Bloomfield, A. L., and Harrop, G. A., Jr.: Bull. Johns Hopkins Hosp., 1919, XXX, 1.

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NOTE.—Since this article went to press a paper has become accessible (E. Schiffer: Monatschrift für Kinderh., 1918, XV, 189) dealing with the same question. The writer did skin tests on 64 children with "influenza." In 61 the test was negative, in three it was weakly positive. Of 28 reexamined during convalescence, three developed positive tests.



